

# Lentiviral reprogramming of human umbilical cord-derived mesenchymal stromal cells towards hepatocyte-like cells

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## Contact person

Karolien Buyl

## Organisation

**Name of the organisation** Vrije Universiteit Brussel (VUB)

**Department** Pharmaceutical and Pharmacological Sciences

**Specific Research Group or Service** In Vitro Toxicology and Dermato-Cosmetology

**Country** Belgium

**Geographical Area** Brussels Region

## SCOPE OF THE METHOD

<b>The Method relates to</b>	Human health
<b>The Method is situated in</b>	Basic Research
<b>Type of method</b>	In vitro - Ex vivo
<b>Specify the type of cells/tissues/organs</b>	umbilical cord

## DESCRIPTION

### Method keywords

human adult stem cells

hepatocyte-like cells

lentiviral reprogramming

umbilical cord

## **Scientific area keywords**

in vitro liver model

Drug-induced liver injury (DILI)

human hepatocyte-like cells

liver enriched transcription factor

human adult stem cells

## **Method description**

Human umbilical cord-derived mesenchymal stromal cells (hUC-MSCs) express several key liver-specific transcription factors as well as hepatic progenitor markers. However, they still lack the hepatocyte nuclear factors 1-alpha (HNF1a) and 4-alpha (HNF4a), indispensable for their reprogramming towards hepatocyte-like cells. This method comprises the reprogramming of hUC-MSCs towards hepatocyte-like cells through HNF1a lentiviral over-expression. Whole genome microarray analysis revealed that the expression of the nuclear receptor retinoid X receptor (RXR) gamma and the nuclear transcription factor HNF4a, in HNF1a-transduced hUC-MSCs, was significantly upregulated compared to the control conditions. This expression was even higher than found in human hepatocytes. The same was observed for the uridine 5'-diphospho-glucuronosyltransferase (UGT) 1A family. Further, a significant upregulation was observed for alpha-fetoprotein (AFP), alpha1-antitrypsin (A1-AT), the phase I biotransformation enzymes cytochrome P450 (CYP) 1A2 and CYP2A6 and the drug transporter multidrug resistance protein (MDR) 1.

## **Lab equipment**

Incubator ( $37 \pm 1^\circ\text{C}$ ,  $90 \pm 5\%$  humidity,  $5.0 \pm 1\%$  CO<sub>2</sub>/air);

Type 2 laminar airflow HEK293T cells;

Ultracentrifuge Water bath ( $37 \pm 1^\circ\text{C}$ );

Inverse-phase contrast microscope;

Pipettes;

Pipettors;

Colorimetric reverse transcriptase assay;

Human hepatocytes;

Affymetrix microarray technologies;

Partek Genomics Suite Software.

## Method status

Still in development

## PROS, CONS & FUTURE POTENTIAL

### Advantages

Persistent expression of HNF1a transcription factor in hUC-MSCs;  
Endogenous induction of HNF4a expression.

### Challenges

Genomic integration of the lentiviral vector.

### Modifications

Usage of a non-integrative reprogramming method e.g. mRNA transfection.

### Future & Other applications

Generation of hepatocyte-like cells for the development of functional human liver-based *in vitro* models for pharmaco-toxicological purposes.

## REFERENCES, ASSOCIATED DOCUMENTS AND OTHER INFORMATION

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